



## A COMPARATIVE STUDY OF THE ADDITIVE ANTI-INFLAMMATORY EFFECT OF TOPICAL NEPAFENAC 0.1% V/S KETOROLAC 0.5% WITH STEROID IN POST-CATARACT SURGERY

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**ABSTRACT** Cataract surgery is relatively an inexpensive surgery but the quality of life solely depends upon whether the first or the second eye is operated. Methods: The study was conducted on 150 patients with features suggestive of significant grade of age related senile cataract were included in three different groups of 50 patients each and were instilled two topical NSAIDs along with topical steroids in post-cataract surgery. The comparison was done amongst the groups for better control of anterior chamber post-operative reaction and pseudophakic cystoid macular edema. Results: There was comparable control of anterior chamber reaction between Nepafenac and Ketorolac but far better control over topical steroid as a monotherapy alone and Nepafenac control of CME was better than use of Topical steroid/ or with topical Ketorolac.

**KEYWORDS :** NSAIDs, Anterior Chamber Reaction. Cystoid Macular Edema.

### INTRODUCTION

The ability to see the world through a good quality vision has been so far the most priced possessions of mankind. Surveys have shown that sight is the sense that people most fear losing vision. <sup>[1]</sup> Cataract surgery is relatively an inexpensive surgery but the quality of life solely depends upon whether the first or the second eye is operated. <sup>[2]</sup> Even as per the health survey carried out in the Canadian community between the years 1994 and 2003, the proportion of older adults who self reported the presence of cataracts had a sharp rise from 14 % to 20%. <sup>[3]</sup>

The most uprisen cause of bilateral blindness developing nations like India is cataract which is responsible for approximately 50-80% of the bilaterally blinds in the country. <sup>[4]</sup> As per the reports of WHO/NPCB survey which had earlier depicted a tremendous burden and backlog of 22 million blind eyes (12 million blind people) in India and 80.1 % are blind due to cataract. <sup>[5]</sup> Minassian and Mehra <sup>[6]</sup> estimated that for India alone 3.8 million people become blind from cataract each year. Globally, the incidence figure is estimated to be alarming around 5 million.

The interventional procedure of removing cataract involves manipulation of ocular tissues, which in turn may lead to post-operative intraocular inflammation. Following surgical manoeuvres intra-ocularly, there occurs the activation of phospholipase A2, which acts by its mechanism to break down cell membrane phospholipids to arachidonic acid. This is further been converted to prostaglandins (PGs) by activation of cyclooxygenase (COX) enzymes via COX-1 and COX-2 pathways. Prostaglandins thus released will lead to local vasodilatation and increased vascular permeability, resulting in a number of symptoms including hyperaemia, miosis, pain, photophobia and diminished visual acuity secondary to cystoid macular edema (CME). <sup>[7]</sup>

Inflammatory cascade inhibition could be achieved at various different locations using agents such as NSAIDs, corticosteroids as the release of arachidonic acid can be stopped by blocking the phospholipase A2 activity using corticosteroids, NSAIDs on the other hand will interfere with the COX-1 and COX-2 activity). Further, NSAIDs also suppress polymorphonuclear cell ability to move and chemotaxis; decreases the activity of inflammatory cytokines and mast cell degranulation. <sup>[8,9,10]</sup>

At present, there are four available topical NSAID preparations, including the phenylacetic acids diclofenac 0.1%, ketorolac 0.5% and bromofenac 0.09%. In addition, is the arylacetic acid, nepafenac 0.1% which unlike the other topical NSAIDs is not a free acid but rather an NSAID prodrug that crosses the cornea

and is bioactivated to the active amfenac moiety by intra-ocular hydrolases. <sup>[11]</sup>

This study is designed based on regulatory guidance to compare the effectiveness of nepafenac 0.1 % to both placebo and a well studied NSAID (Ketorolac 0.5%) for the prevention and treatment of pain and inflammation following cataract surgery.

### METHODS

A prospective, randomized, experimental study was carried out in the Department of Ophthalmology, Sri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh. The study was carried out from 1<sup>st</sup> November 2017 to 31<sup>st</sup> December 2018. The study was conducted on 150 patients with features suggestive of significant grade of age related senile cataract in the In-Patient department of the hospital

### INCLUSION CRITERIA:

- All patients with age related immature senile cataract were included in this study.
- Both males and females patients having age related immature senile cataract above 50 years of age.
- Patients with uncomplicated manual small incision cataract surgery with IOL implantation in the bag.

### EXCLUSION CRITERIA:

- Patients with central corneal opacities or any other corneal dystrophies, pseudoexfoliation of lens, lens induced glaucoma or lens subluxation or dislocation that would affect the treatment response or evaluation.
- Patients with history of uveitis, glaucoma, vascular occlusions like branch retinal vein occlusions, central retinal vein occlusion, Diabetic retinopathy, hypertensive retinopathy, pre-existing macular edema due to any cause.

Patients with history of diabetes, hypertension, bleeding disorders, blood dyscrasias or any other systemic disease, macular pathologies, signs of uveitis or allergic to topical drugs in concern in this study.

A signed informed consent was obtained from all the patients before commencing the study and an ethical clearance was taken from the hospital ethics committee for the conduct of this study. A detailed history of the patient was recorded along with detailed ocular examination been carried out.

### STATISTICAL ANALYSIS

Statistical analysis was performed by the SPSS program for Windows, version 17.0 (SPSS inc Chicago, Illinois, USA ). Data were checked for normality before statistical analysis. Categorical

variables were analysed using either the chi square test or Fisher's exact test. One-way analysis of variance (ANOVA) was used to evaluate the significance of the differences in preoperative and post operative variable. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference.

**PRE-OPERATIVELY-** An topical antibiotic preparation and topical NSAIDS was started a day prior to surgery as assigned to the group. Operative procedure done was manual small incision cataract surgery.

- Patient was put on regular post-operative treatment as follows:
- Tab Ciprofloxacin 750 mg stat and then 500mg HS then 500mg 12 hourly for 5 days
  - E/d Moxifloxacin + Prednisolone acetate 6t/d from post-operative day-1
  - Assigned Eye drop 8 hourly

A detailed examination was done on post-operative day-1 and then the patient was discharged. Follow-up examination was done on post-operative day-1, 7, 28, 90.

**RESULTS**

The study was conducted on a total number of 150 eyes of 150 patients who had cataract. These patients were divided into three groups- A, B and C i.e. each group comprising of 50 patients. Group A patients received Prednisolone Acetate, Moxifloxacin and Nepafenac (0.1%) Group B patients received Prednisolone Acetate, Moxifloxacin and Ketorolac Tromethamine (0.5%) Group C patients Group B patients received Prednisolone Acetate, Moxifloxacin only

**TABLE-1** Distribution of patients in Group A V/s B on the basis of Anterior Chamber Reaction

Anterior Chamber Reaction Cells (Grade)		Group A	Group B	p value	Significance
		Frequency (%)	Frequency (%)		
Post-Operative	0	50 (100%)	50 (100%)	-	-
POD -1	0	32 (64.0%)	30 (60.0%)	0.680	NS
	1	5 (10.0%)	12 (24.0%)	0.062	NS
	2	12 (24.0%)	5 (10.0%)	0.062	NS
POD-7	0	36 (72.0%)	45 (90.0%)	0.022	S
	1	13 (26.0%)	3 (6.0%)	0.006	S
	2	1 (2.0%)	2 (4.0%)	0.558	NS
POD-28	0	47 (94.0%)	49 (98.0%)	0.307	NS
	1	3 (6.0%)	1 (2.0%)	0.307	NS
POD-90	0	50 (100%)	50 (100%)	-	-

**Table-2** Distribution of patients in Group A V/s C on the basis of Anterior Chamber Reaction

Anterior Chamber Reaction Cells (Grade)		Group A	Group C	p value	Significance
		Frequency (%)	Frequency (%)		
Post-Operative	0	50 (100%)	50 (100%)	-	-
POD -1	0	36 (72.0%)	30 (60.0%)	0.007	S
	1	6 (12.0%)	5 (10.0%)	0.249	NS
	2	7 (14.0%)	3 (6.0%)	0.075	NS
POD-7	0	36 (72.0%)	30 (60.0%)	0.002	S
	1	10 (20.0%)	6 (12.0%)	0.017	S
	2	4 (8.0%)	13 (26.0%)	0.004	S
POD-28	0	47 (94.0%)	41 (82.0%)	0.121	NS
	1	3 (6.0%)	9 (18.0%)	0.065	NS
POD-90	0	50 (100%)	50 (100%)	-	-

**Table-3** Distribution of patients in Group B V/s C on the basis of Anterior Chamber Reaction

Anterior Chamber Reaction Cells (Grade)		Group B	Group C	p value	Significance
		Frequency (%)	Frequency (%)		
Post-Operative	0	50 (100%)	50 (100%)	-	-
POD -1	0	30 (60.0%)	30 (60.0%)	-	-
	1	12 (24.0%)	9 (18.0%)	0.461	NS

POD-7	2	5 (10.0%)	3 (6.0%)	0.461	NS
	3	3 (6.0%)	8 (16.0%)	0.110	NS
	0	45 (90.0%)	36 (72.0%)	0.022	S
POD-28	1	3 (6.0%)	4 (8.0%)	0.695	NS
	2	2 (4.0%)	10 (20.0%)	0.014	S
POD-90	0	49 (98.0%)	41 (82.0%)	0.016	S
	1	1 (2.0%)	9 (18.0%)	0.008	S
POD-90	0	50 (100%)	50 (100%)	-	-

**TABLE-4** Distribution of patients in Group A V/s B on the basis of post-operative Cystoid Macular Edema

CME (Cystoid Macular Edema)	Total Patients	CME		p value
		Present	Absent	
Group A	n=50	0	50 (100%)	1.000
Group B	n=50	1	49 (98%)	

**TABLE-5** Distribution of patients in Group A V/s C on the basis of post-operative Cystoid Macular Edema

CME (Cystoid Macular EDEMA)	Total Patients Frequency	CME		p value
		Present	Absent	
Group A	n=50	0	50 (100%)	0.495
Group C	n=50	2	48 (96%)	

**TABLE-6** Distribution of patients in Group B V/s C on the basis of post-operative Cystoid Macular Edema

CME (Cystoid Macular Edema)	Total Patients Frequency	CME		p value
		Present	Absent	
Group B	n=50	1	49 (98%)	1.000
Group C	n=50	2	48 (96%)	

**DISCUSSION**

In this present study, 150 patients of cataract were selected. The drugs were started from day-1 post operatively, three times a day and continued for 28 days thereafter.

A study by Jiro Numaga <sup>[12]</sup> (2011) found that the cure rate on Day-14 after surgery was 71.4% in the Nepafenac group and 28.6% in Group-C, showing a significant difference in control of anterior chamber reaction between groups. The Nepafenac group demonstrated higher control of anterior chamber reaction than those in the placebo group, with a significant difference in cure rates on Day-7 and 14 post-operatively.

The results were similar to the present study which showed 72% control of anterior chamber reaction at POD-1 and POD-7 in the Nepafenac group and 60% in Group-C (p=0.028 and p=0.035 respectively) which shows statistical significance. Thus, Nepafenac was more effective in controlling post-cataract anterior chamber reaction as compared to Group-C using topical steroids only.

In a study done by Wolf et al <sup>[13]</sup> (2007) involved 450 patients and showed that there was a decreased incidence of CME (p=0.035) among the group receiving Nepafenac 0.1% and Prednisolone.

In present study, there was no case incidence of CME in patients receiving Nepafenac.

**CONCLUSION**

The present study was undertaken to compare the anti-inflammatory and analgesic effect of Nepafenac 0.1% with Ketorolac 0.5% after cataract surgery as well as to compare the additive anti-inflammatory effect of Nepafenac 0.1% and Ketorolac 0.5% with steroid in post-cataract surgery.

- 150 patients were randomly divided into three groups comprising of 50 patients each in the age group of 50-85 years with a mean age of the mean age was 60.14 ± 5.99, 59.76 ± 8.41 and 58.50 ± 6.42 years in Group A, B & C respectively.
- This study shows that Ketorolac 0.5% is more effective for relief of anterior chamber reaction than Nepafenac 0.1%.
- This study also demonstrates that Nepafenac 0.1% is superior

to Group C for prevention and treatment of ocular inflammation resulting from cataract surgery and so is the case with Ketorolac 0.5% use in comparison with Group C which has its superior role in controlling the ocular pain and anterior chamber reaction in a better way than steroids alone.

- Moreover, combination topical NSAID/Steroid therapy in the setting of acute, visually significant pseudophakic CME appears to be more beneficial in its prevention over monotherapy alone when a combination of NSAID and steroid is used post cataract surgery giving an additional anti-inflammatory effect.

#### LIMITATIONS OF THE STUDY

The sample size was 150 patients, so more patients could have been recruited for this study. The surgical technique used in this research was manual SICS only. The effects of these topical NSAIDs in other surgical techniques such as phacoemulsification, ECCE was not evaluated.

#### FINANCIAL DISCLOSURE- Nil

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